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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/799,372	03/12/2004	Jeffrey S. Mumm	15060-58	7301

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EXAMINER
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BERTOGLIO, VALARIE E

ART UNIT	PAPER NUMBER
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1632

NOTIFICATION DATE	DELIVERY MODE
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01/11/2008

ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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**Office Action Summary**

Application No.

10/799,372

Applicant(s)

MUMM ET AL.

Examiner

Valarie Bertoglio

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 11/16/2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 31,33,34,36 and 43-51 is/are pending in the application.
- 4a) Of the above claim(s) \_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 31,33,34,36,43-51 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 12 March 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/16/2007 has been entered.

Claims 1-30,32,35 and 37-42 are cancelled. Claims 43-51 have been added. Claims 1-30,32,35 and 37-51 are pending and under consideration in the instant office action.

### ***Claim Objections***

The objections to claims 33 and 34 are withdrawn in light of Applicant's amendments to the claims.

### ***Claim Rejections - 35 USC § 112-1<sup>st</sup> paragraph***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

### ***Written Description***

The rejection of claims 38-40 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is withdrawn.

The claims were previously regarded as lacking written description because in the instant case regulatory DNA sequences that drive specific expression to skeletal, cardiac, bone or cartilage cells of a

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medaka or zebrafish were not supported. While it was previously noted that non-fish promoters were often found to be silenced or misexpressed in transgenic fish rendering the art unpredictable as to whether various nonfish promoters would work effectively in fish, this is no longer a general rule presumed to be true of all nonfish promoters because since the time of filing many mammalian promoters have been shown active with fidelity in fish. Applicant has provided numerous examples of promoters in *Xenopus*, mouse and human that are specifically expressed in the claimed tissues.

Claims 44,47-51 are newly rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. 37 CFR 1.118 (a) states that "No amendment shall introduce new matter into the disclosure of an application after the filing date of the application".

Claims 44 and 50 lack written description because in the instant case the glial, pancreatic and kidney specific expression is not supported by the specification. Applicant is claiming a fish wherein the critical element of the invention is the expression in a specific subset of cells of the fish. The specification contemplates tissue or cell-type specific expression including heart, muscle, neural, skeletal and cartilaginous tissues. The specification fails to contemplate, however, expression in glial cells, pancreas, or kidney.

The newly added claims 48 and 51 contain the terminology "in cis" and "in trans", respectively". Literal support for this terminology is not found in the specification.

MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. In re Rasmussen, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed. If a claim is amended to include subject matter, limitations, or

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terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application. MPEP 2163.06 further notes "When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved. Applicant should therefore specifically point out the support for any amendments made to the disclosure" (emphasis added).

#### *Enablement*

The rejection of claims 31-42 under 35 U.S.C. 112, first paragraph, as lacking enablement for the full breadth of the claims is withdrawn in amendments to the claims. The claims now require the use of a minimal promoter in the transgene construct.

#### *Claim Rejections - 35 USC § 112-2<sup>nd</sup> paragraph*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The previous rejection of claims 35,37 and 41-42 under 35 USC 112, 2<sup>nd</sup> paragraph is withdrawn in light of Applicant's cancellation of the claims.

Claims 31,33-34,36,43-51 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 31 is unclear as written. The claim requires operable linkage of a gene product to a regulatory DNA sequence. It is unclear if Applicant intends some sort of linkage between a protein and a DNA or if the claim is intended to require operable linkage between the regulatory DNA sequence and a gene encoding a gene product. Claims 33-34,36,43 and 44 depend from claim 31.

Suggested and more succinct language for claim 31 would include "A transgenic fish selected from the group consisting of zebrafish and medaka fish, whose genome comprises a transgene comprising

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a gene encoding a gene product wherein the gene product is i) an ablation promoting moiety or ii) a coupled expression system consisting of an ablation promoting moiety linked to a cellular reporter protein that facilitates detection of cells expressing the transgene, wherein the ablation promoting moiety comprises at least one component of a pro-drug conversion system, and wherein the gene is operably linked to a regulatory DNA sequence including at least a promoter element that regulates the expression of the gene encoding the gene product such that the gene product is expressed in a reproducible spatial and temporal pattern in the fish.

Claim 36 is unclear because it is not known what is meant by the phrase "cell specific expression". It is not known if the claim is referring to expression in a single, specific cell or a specific cell "type" such that multiple cells of a single "type" express the transgene. If the latter is the case then the phrase should read "cell-type specific".

Claim 43 is unclear as to whether "a transgene encoded ablation promoting moiety, or a transgene encoded ..." recited in lines 2-3 is the same as that of parent claim 31 or if it is referring to another distinct transgene.

Claim 45 is unclear as written. The claim requires operable linkage of a gene product to a minimal promoter element. It is unclear if Applicant intends some sort of linkage between a protein and a DNA or if the claim is intended to require operable linkage between the regulatory DNA sequence and a gene encoding a gene product. Claims 46-47 depend from claim 45.

Claim 46 is unclear as to whether "a transgene encoded ablation promoting moiety, or a transgene encoded ..." recited in lines 2-3 is the same as that of parent claim 45 or if it is referring to another distinct transgene.

Claim 48 is unclear as written. The claim requires operable linkage of a gene product to a minimal promoter and UAS sequence. It is unclear if Applicant intends some sort of linkage between a

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protein and a DNA or if the claim is intended to require operable linkage between the minimal promoter and UAS sequence and a gene encoding a gene product. Claims 49-50 depend from claim 48.

The phrase "the UAS being specifically bound....expression pattern to the transgene encoded product" (lines 7-11) in claim 48 renders the claim unclear. It is not known if the claim is requiring that the UAS be actively bound by an activator or if it is describing a property of the UAS.

The phrase "...and whereby the transcriptional activator...and thereby to the UAS-linked transgene encoded product" at lines 13-17 of claim 48 is unclear. The phrase does not set forth what "in cis" is with respect to. It is not clear how a transcriptional activator can be part of the transgene since the activator is a protein. The phrase "linked to its own regulatory DNA" is unclear because it is not known what is encompassed by the term "own". It is not clear how the transcriptional activator can be part of the transgene itself *and* be operably linked, presumably, to a different promoter. The Examiner interprets the phrase as meaning "whereby the transcriptional activator is operably linked to a second regulatory DNA sequence comprising a promoter that confers a specific reproducible spatial and temporal expression pattern to the transcriptional activator and thereby to the UAS-linked transgene".

Claim 51 is unclear as written. The claim requires operable linkage of a gene product to a minimal promoter and UAS sequence. It is unclear if Applicant intends some sort of linkage between a protein and a DNA or if the claim is intended to require operable linkage between the minimal promoter and UAS sequence and a gene encoding a gene product.

The phrase "the UAS being specifically bound....expression pattern to the transgene encoded product" (lines 7-11) in claim 51 renders the claim unclear. It is not known if the claim is requiring that the UAS be actively bound by an activator or if it is describing a property of the UAS.

It is also noted that the phrase "whereby a single UAS-linked transgenic line....UAS-linked transgene encoded product" (lines 17-19) appears to pertain to subject matter outside the realm of the claim and its relevance is not clear.

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It is noted that the structure intended by use of the term “in cis” and “in trans” in claims 48 and 51 is unclear. The specification appears to have figurative support for what may be intended by claim 51. However, the structure claimed in 48 does not appear to be supported by the specification. The Examiner is familiar with the art-accepted definitions of “cis” acting sequences and “trans” acting factors. However, this definition does not appear to fit the claims as written. Clarification is requested.



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*Conclusion*

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Valarie Bertoglio whose telephone number is (571) 272-0725. The examiner can normally be reached on Mon-Thurs 5:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Valarie Bertoglio, Ph.D./  
Primary Examiner  
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